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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,232	12/12/2003	Yosser Ben Achour	02356.0087	4579

22852 7590 06/14/2005

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,232	BEN ACHOUR ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

A. Claims 1, 3, 16-19 and 20-22 are drawn to a protein and an immunogenic composition and vaccinating composition comprising said protein classified in class 424, subclass 184.1.

B. Claims 2-3, 16-19 and 20-22 are drawn to a *Leishmania* protein and an immunogenic composition and vaccinating composition comprising said protein, classified in class 424, subclass 269.1

C. Claims 1, 4-6, 16-19 and 20-22 are drawn to a recombinant polypeptide and an immunogenic composition and vaccinating composition comprising said polypeptide, classified in class 435, subclass 69.1.

D. Claims 2, 4-6, 16-19 and 20-22 are drawn to a recombinant *Leishmania* protein and an immunogenic composition and vaccinating composition comprising said protein, classified in class 536, subclass 23.1.

E. Claims 7-12, 16-19 and 20-22 are drawn to a recombinant nucleic acid, vector, and an immunogenic composition and vaccinating composition comprising said nucleic acid classified in class 435, subclass 320.1.

F. Claim 13 is drawn to the use of a nucleic acid probe, classified in class 536, subclass 24.32.

G. Claim 14 is drawn to a nucleotide primer, classified in class 536, subclass 24.3.

H. Claims 15 and 30-31 are drawn to an antibody and pharmaceutical composition, classified in class 424, subclass 130.1.

I. Claims 23-25 are drawn to a method for screening molecules, classified in class 435, subclass 258.3.

J. Claims 26-28 and 32-33 are drawn to the use of one or more protein disulfide isomerase inhibitors and pharmaceutical compositions, classified in class 536, subclass 24.5.

K. Claim 29 is drawn to the use of bacitracin, classified in class 530, subclass 320.

L. Claims 34-35 are drawn to an in vitro method for diagnosing an infection and diagnostic kit, classified in class 435, subclass 7.1.

2. The inventions are distinct, each from the other because of the following reasons:

(i) Inventions A, B, C, and D are patentably different products. The inventions are distinct, each from the other because of the following reasons: Although there are no provisions under the section for "Related Inventions" in M.P.E.P. 806.05 for inventive groups that are directed to different products; restriction is deemed to be proper because these products appear to constitute patentably distinct inventions. Group A is drawn to a protein, Group B is drawn to a *Leishmania* protein, Group C is drawn to a recombinant protein and Group D is drawn to a recombinant *Leishmania* protein. The groups are directed to proteins which are distinct physically, structurally and

functionally, and are therefore patentably distinct, each group from the other. For instance, the protein of Group B is a *Leishmania* protein which unlike the protein of Group A, even though both contain one site identical to the potential active site of a protein from the protein disulfide isomerase (PDI) family. Moreover, proteins comprising the active site (Cys-Gly-His-Cys) is found in other parasitic protozoa such as *Cryptosporidium parvum* (see Blunt et al., 1996. Gene. Vol. 181, pages 221-223). Thereby, making the protein of Group A distinct from the protein of Group B. The recombinant proteins of groups C and D are capable of triggering an immunological reaction against an epitope of LmPDI, unlike the proteins of group A and B. However, the recombinant proteins of groups C and D are also distinct each from the other because only Group D requires that the recombinant protein by a Leishmania protein, unlike group C. Therefore, one protein is not required to practice the other. Each group comprises separate and distinct proteins that are not disclosed as being essential to the utility of the invention.

Furthermore, searching the inventions of groups A-D would impose a serious search burden. The inventions have a separate status in the art as shown by their distinct structure. Thus different proteins require different searches. An amino acid sequence search of the full-length protein is not necessary for a determination of novelty and unobviousness of another unrelated protein. Moreover, a search of group A is not required to identify the protein of group D. Furthermore, the protein of group B may be known even if the protein of group C is novel. In addition, the technical literature search for the recombinant *Leishmania* protein of group D and the protein of

group A are not coextensive, e.g., the protein of group A may be characterized in the technical literature prior to discovery of or sequence of group D.

(ii) The protein of group A, the *Leishmania* protein of group B, the recombinant protein of group C and the recombinant *Leishmania* protein of group D and nucleic acid of group E are patentably distinct inventions for the following reasons. Proteins are composed of amino acids, and nucleic acids are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a protein and a nucleic acid is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded protein. In the present claims, a nucleic acid of group E does not necessarily encode any particular protein of group A, B, C or D. For example, as disclosed in the specification, SEQ ID NO: 2 is 447 amino acids in length, whereas the nucleic acid requires only 30 nucleotides (which would encode at most a polypeptide of 10 amino acids in length). Furthermore, the information provided by the nucleic acid of group E could be used to make a materially different polypeptide than that of group A, B C or D. For example, a nucleic acid which hybridizes to SEQ ID NO: 1, even under stringent conditions, encompasses molecules which contain point mutations, splice sites, frameshift mutations or stop codons which would result in use of a different open reading frame, and thus encode a protein that lacks any significant structure in common with SEQ ID NO. 2. In addition, while the proteins of group A, B, C or D can made by methods using some, but not all, of the nucleic acids that fall within the scope of group

E, it can also be recovered from a natural source using by biochemical means. For instance, the proteins can be isolated using affinity chromatography. For these reasons, the inventions of groups A, B, C, or D and E are patentably distinct.

Furthermore, searching the inventions of groups A, B, C, D and E together would impose a serious search burden. In the instant case, the search of the proteins and the nucleic acids are not coextensive. The inventions of Groups A, B, C, D and E have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to proteins which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. In addition, the polypeptide claims include proteins having 40% identity to LmPDI. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of nucleic acids as claimed extend beyond the polynucleotide that encodes the claimed proteins as explained above; furthermore, a search of the nucleic acid molecules would require an oligonucleotide search, which is not likely to result in relevant art with respect to the proteins of group A, B, C and D. As such, it would be burdensome to search the inventions of groups A, B, C, D and E together.

(iii) The proteins of group A-D and the antibody of group H are patentably distinct for the following reasons: In this instance the antibody of group H encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs) that function to bind an epitope, which is unlike groups A-D. Thus the proteins of group A-D and the antibody of group H are structurally distinct molecules; any relationship between the protein of group A-D and an antibody of group H is dependent upon the correlation between the scope of the protein that the antibody binds and the scope of the antibodies that would be generated upon immunization with the protein.

In this case, the proteins of group A-D is a large molecule which contains potentially hundreds of regions to which an antibody may bind, whereas the antibody of group H is defined in terms of its binding specificity to a LmPDI. Thus immunization with the proteins of group A-D would result in the production of antibodies outside the scope of group H (i.e., antibodies that bind to regions other than residues LmPDI). Furthermore, an antibody of group H would not specifically bind all of the proteins of group A-D because the proteins of group A-D are not required to include the LmPDI region to which the antibody binds. Therefore the proteins and antibody are patentably distinct.

Furthermore, searching the inventions of group A-D and group H would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A protein and an antibody which binds to the protein

require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of group H. Furthermore, antibodies which bind to an epitope of a protein of group A-D may be known even if a protein of group A-D are novel. Similarly, a search for the residues of LmPDI is required to determine the novelty and nonobvious of the antibodies of group H, however such a search is not required or sufficient to identify all of the proteins of groups A-D. In addition, the technical literature search for the proteins of group A-D and the antibody of group H are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

(v) The nucleic acid of group E and the antibody of group H are patentably distinct for the following reasons. The antibody of group H includes, for example, IgG molecules which comprise 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs). A nucleic acid is composed of structurally distinct molecules; any relationship between a nucleic acid and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a nucleic acid of group E will not encode an antibody of group H, and the antibody of group H cannot be encoded by a

polynucleotide of group E. Therefore the antibody and nucleic acids are patentably distinct.

The antibody and nucleic acid inventions have a separate status in the art as shown by their different classifications. Furthermore, searching the inventions of group E and group H would impose a serious search burden since a search of the polynucleotide of group E is would not be used to determine the patentability of an antibody of group H, and vice-versa.

(vi) Inventions F, G, H and J are patentably different products and are patentably distinct for the following reason, they have different structures and different uses. In this case, Group F is drawn to a probe which specifically hybridizes under stringent conditions to SEQ ID NO:2; Group G is drawn to a primer which allows for the specific amplification of SEQ ID NO:1; Group H is drawn to an antibody which specifically recognizes LmPDI; and Group J is drawn to a protein-disulfide isomerase (PDI) inhibitor. Thus, the products encompass structurally distinct molecules. Each group has a different function, effect and is capable of use without the other. For instance, the antibody product of Group H can specifically recognize LmPDI as opposed to the products of group F,G and J which cannot. No other group can specifically hybridizes under stringent conditions to SEQ ID NO:2. Each group has a different structure, produces different effects and has a different function from the other group. Therefore, the products of the inventions are distinct as claimed.

Furthermore, searching the inventions of groups F, G, H and J would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. An antibody which specifically recognizes LmPDI require a different search, than the probe, primer or PDI inhibitor. A search drawn to hybridization techniques is NOT necessary for a determination of novelty and unobviousness of the probe. However, such a search is not required to identify the antibodies of group H. Furthermore, antibodies which specifically recognizes LmPDI may be known even if the primer of group G is novel. Similarly, an amino acid sequence search for the residues of LmPDI is required to determine the novelty and nonobvious of the antibodies of group III, however such a search is not required or sufficient to identify the PDI inhibitor. In addition, the technical literature search for the antibody of group H and the primer, probe or inhibitor are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of primers, probes and PDI inhibitors.

(vii) Inventions A,B,C, D and E and either of I and L are unrelated because the products of groups A,B, C, D and E is not used or otherwise involved in the methods of group I and L.

(viii) Inventions I and L are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that these methods would be used together.

The method for screening molecules that are susceptible of inhibiting the growth of Leishmania major (group I) and the in vitro method for diagnosing an infection by a parasite (group L) are all unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using a structurally and functionally divergent material. Moreover, the methodology and materials necessary for diagnosis of an infection by a parasite differ significantly. Diagnosis uses the antibody, and detects the antibody. Screening evaluates the capacity of a molecule to inhibit the activity of LmPDI. Therefore, each method is divergent in materials and steps. For these reasons the inventions I and L are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups I and L have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups I and L together.

(ix) Inventions F,G,J,K and either of I and L are unrelated because the products of groups F, G, J or K is not used or otherwise involved in the methods of group I and L.

3. The inventions of Groups A-L have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search any combination of the inventions of Groups A-L together.

4. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

5. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 1, 2005